REMARKS

Claims 23, 24, 28, 39-42 and 44-54 remain in this application. Claim 43 has been canceled as being an apparent duplicate of claim 42. Claim 44 has been amended to depend properly from claim 42 and claims 53 and 54 have been amended to correct inadvertent typographical errors.

Objections Under 37 CFR 1.75(c)

The Action has objected to claims 43 and 53 under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of the previous claim. Applicants have canceled claim 43 as being duplicative of claim 42 and amended claim 44 to depend properly from claim 42. Applicants respectfully argue that claim 53 is in proper dependent form as it differs from claim 52 in that claim 53 does not include PEG-200, PEG-300 or PEG-400 as part of the Markush group, and therefore would be of arguably narrower scope.

Indefiniteness Under 35 USC § 112, 2nd Paragraph

The Action has rejected claim 23 under 35 USC § 112, 2nd paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Action considers the term "derivative" to be indefinite. As previously stated in Applicants' Response dated October 2, 2003, the term "derivative" is well known in the art. In accordance with claim 23, the derivatives have a volume weighted mean particle size in the range of 0.01 to 0 micrometers and are insoluble or poorly soluble in hydrophobic liquids. Derivatives of paclitaxel and camptothecin are antineoplastic agents and derivatives of acyclovir are antiviral agents, as described in the original specification at page 16, lines 13-22.

Anticipation Under 35 USC § 102(b)

GB 1,527,638

The Action has rejected claim 24 under 35 USC § 102(b) as being anticipated by GB 1,527,638 ("GB"). The Action states that GB discloses a niclosamide suspension, which "contains niclosamide (particle size of 2 to 20 microns) in sesame oil, polyoxyethylene-sorbitan monooleate, and 10% n-butanol." The Action further notes that lecithin is used in the examples and the suspension is administered to an animal. (Action, p. 4). The Action also notes that the term "wherein upon addition of said composition to a fluid aqueous medium..." is intended use.

Applicants submit that GB does not anticipate claim 24 because GB discloses only a suspension of niclosamide or salts thereof, not of any other water-insoluble biologically active substances. Therefore, GB does not anticipate suspensions of any other biologically active substances other than niclosamide and salts thereof. GB also does not disclose a non-aqueous suspension that self-disperses in a fluid aqueous medium such as water. GB only discloses a non-aqueous suspension. Applicant also submits that self-dispersion of the claimed composition in a fluid aqueous medium is not inherent to an oil suspension. GB certainly does not teach self-dispersion of an oily suspension in water. Thus, absent specifically recited elements of the claim in question, GB cannot anticipate claim 24.

US 3,185,625 (Brown)

The Action has rejected claim 24 under 35 USC § 102(b) as being anticipated by US 3,185,625 ("Brown"). The Action states that Brown discloses injectable substances, wherein "drug particles of 1.4-35 [sic] millimicrons are encapsulated with cellulose or synthetic polymers", then "suspended in oil (mineral oil) and emulsified with water." The Action further notes that the surfactants taught are Tween 20 and polyoxyethylene sorbitan monolaurate, and the drugs taught are toxoid, antigens, anti-allergic agents, hormones, and therapeutics. (Action, p. 4).

Applicants submit that Brown does not anticipate claim 24 because Brown discloses only drug particles of 1.5-35 millimicrons, whereas claim 24 encompasses the range from about 0.1 to about 10 micrometers. One of skill in the relevant formulation art would readily recognize that significant differences in chemical and physical properties would arise from differences in particle size of several orders of magnitude. Furthermore, emulsification of the composition described in Brown is accomplished by "rapid agitation" with water (see Brown col. 3, lines 50-51). Brown does not disclose self-emulsification or self-dispersion. The present invention specifically does not require agitation for emulsification.

Obviousness Under 35 USC § 103(a)

US 3,185,625 (Brown) and JP 360174726 (JP)

The Action has rejected claim 23 under 35 USC § 103(a) as being unpatentable over Brown in view of JP 360174726 ("JP"). The Action states that Brown discloses injectable substances, wherein "drug particles of 1.5-35 millimicrons are encapsulated with cellulose or synthetic polymers", then "suspended in oil (mineral oil) and emulsified with water." The Action further notes that the surfactants taught are Tween 20 and polyoxyethylene sorbitan monolaurate,

and the drugs taught are toxoid, antigens, anti-allergic agents, hormones, and therapeutics. The Action also states that JP teaches "the use of a peptide hormone (insulin) in an injectable formula to treat diabetes." (Action, p. 5). The Action contends that it would have been obvious to one of ordinary skill in the art at the time of the invention to look to the teaching of JP and utilize insulin in Brown's formulation. The Action further states that "a skilled artisan would expect similar results since brown teaches the suitability of hormones in the formulation." (Action, pp. 5-6).

First, there is no evidence that Brown in view of JP would suggest to or motivate one of ordinary skill in the art to do any of the above. Brown discloses only drug particles of 1.5-35 millimicrons, whereas claim 24 encompasses the range from about 0.1 to about 10 micrometers. One of skill in the relevant formulation art would readily recognize that significant differences in chemical and physical properties would arise from differences in particle size of several orders of magnitude. Furthermore, emulsification of the composition described in Brown is accomplished by "rapid agitation" with water (see Brown col. 3, lines 50-51). Brown does not disclose self-emulsification or self-dispersion. JP does not teach a self-dispersing insulin suspension. Thus, there would have been no motivation for one skilled in the art to combine Brown and JP to do any of the above.

Second, there is nothing in Brown in view of JP that would provide a reasonable expectation of success in the practice of the methods of the present invention. Brown requires the additional step of encapsulating the particles in a protective coating. The present invention as set forth in claim 24 does not require such a step. There is nothing in either Brown or JP to suggest the omission of the encapsulating step. In addition, since neither Brown nor JP discuss a self-dispersing non-aqueous suspension, the combination of these references would not lead to the composition described in claim 24.

Finally, even if combined, Brown and JP do not teach all of the claim limitations of claim 24. Neither reference teaches a self-dispersing composition. One skilled in the art would not find it obvious to make a non-aqueous suspension that would be self-dispersing in an aqueous medium.

GB 1,527,638 (GB) and US 5,342,625 (Hauer et al.)

The Action has rejected claims 23 and 28 under 35 USC § 103(a) as being unpatentable over GB in view of US 5,342625 ("Hauer et al."). The Action states that GB discloses a

"'preconcentrate niclosamide suspension" which "contains niclosamide (particle size of 2 to 20 microns) in sesame oil, polyoxyethylene-sorbitan monooleate, and 10% n-butanol." The Action further notes that lecithin is used in the examples, that the suspension is administered to an animal to treat parasitic infections and that oral adminstration is disclosed. The Action states that Hauer et al. teach "a pharmaceutical composition containing cyclosporin, an antiparasitic, in a preconcentrate or microemulsion form. The formulation contains a hydrophilic phase, a lipophilic phase, and a surfactant." The Action also notes that the composition "may be formulated for oral administration in a unit dosage form such as a hard or soft gelatin." (Action, p. 6). The Action contends that is would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of GB and Hauer et al. and utilize a gelatin capsule. It would have been obvious "to look to the teaching of GB and utilize an oily suspension in Hauer's formulation. One would be motivated to do so since GB teaches the oily suspensions have better resorption of the medicament than the aqueous suspension, and give better plasma concentration." (Action, pp. 6-7).

First, there is no evidence that GB in view of Hauer et al. would suggest to or motivate one of ordinary skill in the art to do any of the above. GB discloses only a suspension of niclosamide or salts thereof, not of any other water-insoluble biologically active substances. GB also does not disclose a non-aqueous suspension that self-disperses in a fluid aqueous medium such as water. GB only discloses a non-aqueous suspension. Hauer et al. disclose only a microemulsion preconcentrate containing cyclosporin. No other active substance is disclosed by Hauer et al. Furthermore, GB teaches a "preconcentrate" that requires further dilution prior to administration. The present invention does not require further dilution before administration. Thus, there would have been no motivation for one skilled in the art to combine GB and Hauer et al. to do any of the above.

Second, there is nothing in GB in view of Hauer et al. that would provide a reasonable expectation of success in the practice of the methods of the present invention. Since GB only discusses the active substance niclosamide and its salts, and Hauer et al. only discuss the active substance cyclosporin, the combination of these references would not lead to the compositions described in claims 23 and 28. The further step of dilution of the preconcentrate taught by GB is not required by the present invention, thus further minimizing a reasonable expectation of success in the practice of the methods of the present invention.

Finally, even if combined, GB and Hauer et al. do not teach all of the claim limitations of claims 23 or 28. Neither reference teaches a self-dispersing composition. One skilled in the art would not find it obvious to make a non-aqueous suspension that would be self-dispersing in an aqueous medium.

US 5,814,324 (Sato et al.) and GB 1,527,638 (GB) or US 3,185,625 (Brown)

The Action has rejected claims 23, 24 and 39-54 under 35 USC § 103(a) as being unpatentable over US 5,814,324 ("Sato et al.") in view of GB or Brown. The Action contends that Sato et al. teach "a method of preparing injectable compositions containing the anti-fungal itraconazole", wherein "the 0.1g compound is either dispersed or dissolved in 10g of soybean oil, 10g lecithin, and 2.5g of glycerol" and "the fat particles have a mean size of 45 nm." However, Sato et al. do not teach the particle size of the drug. The Action states that GB discloses a "'preconcentrate niclosamide suspension" which "contains niclosamide (particle size of 2 to 20 microns) in sesame oil, polyoxyethylene-sorbitan monooleate, and 10% n-butanol." The Action further notes that lecithin is used in the examples, that the suspension is administered to an animal to treat parasitic infections and that oral adminstration is disclosed. The Action also states that GB teaches "the drug particles size is usually smaller than 2 microns to prevent particle growth, which prevents good resorption of the drug." (Action, pp. 7-8). The Action states that Brown discloses injectable substances, wherein "drug particles of 1.5-35 millimicrons are encapsulated with cellulose or synthetic polymers", then "suspended in oil (mineral oil) and emulsified with water." The Action further notes that the surfactants taught are Tween 20 and polyoxyethylene sorbitan monolaurate, and the drugs taught are toxoid, antigens, anti-allergic agents, hormones, and therapeutics. The particle size of the encapsulated drug is "small enough to pass through a hypodermic injection." (Action, p. 8). The Action asserts that its would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Sato et al. and GB and utilize the instant particle size and that one would be motivated to do so because GB "teaches that the instant particle size prevents particle growth and particle growth prevents good resorption of the drug." Furthermore, the Action states that one would be motivated to combine the teachings of Sato et al. and Brown "since Brown teaches the particle size of the drug, which is in the instant range, should be small enough to pass through the hypodermic needle." (Action, pp. 8-9).

First, there is no evidence that Sato et al. in view of GB or Brown would suggest to or motivate one of ordinary skill in the art to do any of the above. Even though Sato et al. disclose a non-aqueous suspension or solution containing itraconazole, they do not teach a self-dispersing suspension. In order to effect a rough emulsification in water, Sato et al. teaches the use of a emulsifying apparatus. (Sato et al., col. 21, line 67 – col. 22, line 5). Sato et al. do not discuss self-dispersing non-aqueous suspensions. Brown discloses only drug particles of 1.5-35 millimicrons, whereas claims 23, 24 and 39-54 encompass the range from about 0.1 to about 10 micrometers. One of skill in the relevant formulation art would readily recognize that significant differences in chemical and physical properties would arise from differences in particle size of several orders of magnitude. Furthermore, emulsification of the composition described in Brown is accomplished by "rapid agitation" with water (see Brown col. 3, lines 50-51). Brown does not disclose self-emulsification or self-dispersion. GB discloses only a suspension of niclosamide or salts thereof, not of any other water-insoluble biologically active substances. Furthermore, GB teaches a "preconcentrate" that requires further dilution prior to administration. The present invention does not require further dilution before administration. GB also does not disclose a non-aqueous suspension that self-disperses in a fluid aqueous medium such as water. GB only discloses a non-aqueous suspension. Thus, there would have been no motivation for one skilled in the art to combine GB and Hauer et al. to do any of the above.

Second, there is nothing in Sato et al. in view of either GB or Brown that would provide a reasonable expectation of success of the methods of the present invention. Brown requires the additional step of encapsulating the particles in a protective coating. The present invention as set forth in claims 23, 24 and 39-54 does not require such a step. There is nothing in either Brown or JP to suggest the omission of the encapsulating step. Furthermore, GB teaches a "preconcentrate" that requires further dilution prior to administration. The present invention does not require further dilution before administration. Moreover, since none of Sato et al., Brown or GB discuss a self-dispersing non-aqueous suspension, the combination of these references would not lead to the compositions described in claims 23, 24 and 39-54.

Finally, even if combined, Sato et al., GB and Brown do not teach all of the claim limitations of claims 23 or 28. None of the references teaches a self-dispersing composition. One skilled in the art would not find it obvious to make a non-aqueous suspension that would be self-dispersing in an aqueous medium.

CONCLUSION

Applicants respectfully submit that the present application complies with 37 C.F.R. §1.121. Applicants believe no further fee is due at this time; however, the Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Reference Number: 28069-538 (Customer Number: 35437).

If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

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